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The Honorable Bill Cassidy, MD
Ranking Member
Committee on Health, Education, Labor, and Pensions
United States Senate
Washington, DC 20510-6300

Dear Dr. Cassidy:

On behalf of the Association of American Medical Colleges (AAMC), I write in response to your March 13 [request for information](#) (RFI) regarding proposals to reform diagnostic regulation, specifically regulation of Laboratory Developed Tests (LDTs). The AAMC appreciates the opportunity to highlight our concerns with various competing proposals to regulate diagnostic tests developed by academic medical center (AMC) laboratories, and the resulting impact on patient access to care and medical innovation. We also greatly appreciate your willingness to engage stakeholders on ways to improve our nation's health.

The AAMC is a nonprofit association dedicated to improving the health of people everywhere through medical education, health care, medical research, and community collaborations. Its members are all 158 U.S. medical schools accredited by the [Liaison Committee on Medical Education](#); 13 accredited Canadian medical schools; approximately 400 academic health systems and teaching hospitals, including Department of Veterans Affairs medical centers; and more than 70 academic societies. Through these institutions and organizations, the AAMC leads and serves America's medical schools, academic health systems and teaching hospitals, and the millions of individuals across academic medicine, including more than 193,000 full-time faculty members, 96,000 medical students, 153,000 resident physicians, and 60,000 graduate students and postdoctoral researchers in the biomedical sciences. Following a 2022 merger, the Alliance of Academic Health Centers and the Alliance of Academic Health Centers International broadened participation in the AAMC by U.S. and international academic health centers.

Background

For many years, the development and provision of LDTs in the context of clinical care was understood to be outside the scope of FDA regulation, as these tests were designed and used by a single laboratory unlike widely available commercial diagnostic tests, which were regulated by the FDA as medical devices. In October 2014, the FDA released a draft guidance document asserting, contrary to the general understanding of the academic medical community, that LDT oversight was always under the FDA's authority but that the agency had exercised "enforcement discretion" for decades and the agency decided to begin regulating LDTs as medical devices.

The LDTs offered by clinical labs at AMCs had not previously been regulated by the FDA through the existing device regulations, and many AMCs considered this repositioning very concerning. Many LDTs would have been newly subject to regulation as a result of the guidance change, and that would present a host of new challenges. According to the FDA, the purpose of the revised framework was to give the FDA oversight of LDTs “based on risk to patients rather than whether they were made by a conventional manufacturer or a single laboratory.”

The FDA's novel approach to LDTs was developed and released without the significant expertise of and engagement with the academic medicine community. In response to concerns raised by the academic medicine community and many other stakeholders about the impact on patients of making it more difficult to create and administer these tests, the FDA did not finalize the draft guidance, and subsequently several Congresses drafted and introduced multiple versions of proposed legislation to require FDA oversight of LDTs, with the most recent bill, the Verifying Accurate, Leading-edge IVCT Development (VALID) Act of 2021, being incorporated into the Senate Health, Education, Labor, and Pension Committee’s draft FDA user fee reauthorization text, the Food and Drug Administration Safety and Landmark Advancements (FDASLA) Act of 2022. Ultimately, due to the concerns of many stakeholders, the text of the VALID Act failed to be incorporated into law as part of the FDA user fee reauthorization.

AAMC Position on Laboratory Developed Tests

The AAMC believes that LDTs used to inform treatment decisions for patients must be accurate and clinically valid. When the development of LDTs create the possibility for a public health risk of inaccurate or misleading tests, as when LDTs are developed and marketed directly to patients outside both FDA oversight and the highly regulated, exacting environment of an AMC, those tests should be evaluated and addressed. However, we share the concerns of our member AMCs, teaching health systems and hospitals, and clinical laboratories that the FDA’s proposed regulatory scheme would have an immediate and detrimental effect on specialized and patient-centric medical care. Additionally, the FDA’s proposed regulatory framework would interfere with delivering innovative, cutting-edge medical care, negatively impact patients, mire the development of critical new tests in a costly and laborious regulatory process, and quickly overwhelm the ability of the FDA to efficiently review tests submitted for approval. Rather than identifying problematic tests more quickly, this would overrun the agency with submissions, including the many tests which have been used for years to provide critical information to patients’ health care providers.

The AAMC has maintained that AMCs, teaching health systems and hospitals, and the faculty physicians performing LDTs every day on the front line of patient care are best able to determine the most appropriate way to treat patients with important information collected from clinically validated, well-proven, and carefully tailored diagnostic tests. We strongly urge policymakers, including both Congress and the FDA, to partner with academic medicine as it works to deliver timely and innovative patient care, not stifle it.

As the FDA moves to regulate LDTs and Congress considers potential alternatives, the AAMC continues to engage with all stakeholders to find a workable solution and advocate for the continued valuable and critical use of LDTs in the practice of medicine.

Differentiating Academic Medical Center Clinical Labs

Clinical labs in AMCs have unique characteristics that differentiate them from other types of labs that develop and manufacture LDTs. These factors were a large part of why the FDA was comfortable with the development and provision of LDTs in AMCs without FDA regulation for many years.

Key characteristics of academic clinical laboratories (ACLs) include:

- Integration as an integral component of an academic institution which provides direct patient medical care.
- A primary role providing testing and interpretation for the benefit of the patients and clinicians in an affiliated hospital or academic health center as a part of the treatment decision-making process.
- Certification by the Centers for Medicare & Medicaid Services (CMS) through the Clinical Laboratory Improvement Amendments of 1988 (CLIA) program to conduct high-complexity tests.

As a function of the ACL's position in an AMC, its activities are already under many levels of internal and external scrutiny. In addition to the laboratory oversight evidenced by CLIA certification, some states, including New York, have additional requirements. Thus, adding another layer of FDA regulation, although it evaluates different characteristics than existing oversight, could limit access to these tests without meaningful changes in the accuracy or validity of the results.

Key Considerations in the Regulation of LDTs

As Congress and the FDA consider the potential regulation of LDTs, we will continue to prioritize patient access to critical diagnostics and innovative care while working with policymakers to find workable solutions that protect the valuable and essential use of LDTs in academic medicine. Should policymakers and regulators move forward with any form of LDT regulation without providing an exemption for ACLs, several key tenets would help ensure these new regulations are less likely to decrease the number of available tests for patient care which would negatively impact patients' health.

- Any revised regulatory framework must recognize that an overly burdensome system to review LDTs could negatively impact the provision of tailored, high-quality care to patients, and hinder academic medicine in responding quickly to emerging public health risks.

- Without knowing the number of tests that would be affected by a proposed regulatory framework, policymakers are likely to underestimate the burden to an institution developing these tests and the resulting negative impact on patient care. As any new approach is developed, it must also take into account the frequency of modification to new and existing tests, which modifications would require a new approval process, and the rate at which new tests are being developed. This information is critical to accurately estimate the federal and institutional resources needed to implement the revision without negatively impacting patient care.
- Recognizing that identifying rare diseases may require the testing of many individuals, carve-outs for rare disease tests should be based on the incidence or prevalence of disease, not on the number of tests performed.
- A system that recognizes the proven success and validity of certain tests or categories of LDTs is essential in ensuring that the government's resources more effectively target those diagnostic tests that present the most potential risk to patients, including those developed outside an academic medical center without sufficient safeguards or oversight. Any regulation of LDTs should include a wide range of situations under which enforcement jurisdiction or grandfathering is applied to facilitate the continued use of current well-known and well-developed tests without undue burden on the system as a whole.
- The economic impact of institutional compliance with the proposed new regulatory framework for currently administered and newly developed LDTs would be untenable for AMCs, given the cost of guiding even a single test through the FDA premarket approval process. This cost would necessarily lead to institutional decisions not to develop certain diagnostic tests, limiting patient access to innovative and targeted care.

Academic Clinical Laboratory Exemption

Given the integration of test development and administration into the continuum of patient care at AMCs, the many other safeguards these labs are already subject to, and the FDA's retained ability to investigate and remove any test from the market regardless of the entity that develops it, **both FDA and Congress must recognize the need to exempt these academic clinical laboratories from an overly burdensome regulatory framework.**

As part of its proposed rule, the FDA has provided for consideration a definition of "academic medical center" for continuing enforcement discretion at these entities. While the AAMC is fully supportive of the FDA's using general enforcement discretion with respect to tests at AMCs, the definition provided is problematic as it would tend to arbitrarily exclude certain organizations that are unquestionably AMCs for which general enforcement discretion would be appropriate.

FDA Regulatory Framework for Diagnostics

As stated in our December 2023 FDA [comment letter](#), diagnostic testing is a critical element of medical decision-making and, in many cases, commercially available diagnostic tests can provide a health care provider with sufficient information to recommend a treatment plan. However, AMCs serve as quaternary and tertiary facilities, serving patients who often require more tailored, specialized, or specific diagnostic tools. This is where the unique value of LDTs comes into play. These tests, when created in an academic laboratory that is certified for high-complexity testing, meet the needs of patients and providers and fill gaps where commercial products do not, and will never exist. It is only because of these LDTs that many of these patients can receive accurate diagnoses and life-changing medical treatment, including those with rare diseases, genetic and metabolic disorders, emerging infectious agents, pediatric illnesses, and cancer-causing gene mutations.

At AMCs, the development of LDTs is exacting, rigorous, resource-intensive, and an essential component of patient care. While LDTs manufactured outside of academic medical centers have been identified with consumer harm and inaccurate results, **a federal response that makes safe, accurate, and needed LDTs unavailable to patients does not promote public health and welfare.** We are concerned that this proposal establishes a broad, disruptive oversight mechanism that will hinder the ability of AMCs to provide care to patients who need it most.

The AMC laboratory environment provides a higher level of oversight, regulation, engagement between laboratory and clinician, expertise, and focus on specific patient need than do commercial manufacturers of LDTs and thus continued general enforcement discretion with respect to LDTs developed at academic laboratories is warranted. For these reasons, we have urged the FDA to maintain its enforcement discretion for tests that are developed in the highly regulated, specialized AMC environment to allow the agency to focus on those tests being marketed directly to patients without the safeguards and oversight which are already an integral part of LDT development at academic medical centers.

The FDA's proposed new regulatory framework fails to recognize that an overly burdensome system to review LDTs could greatly slow the rate of clinical innovation that is critical to keeping our health care system at the forefront of discovery, providing quality care to patients, and responding quickly to emerging public health risks. The extensive time commitment and the economic impact of institutional compliance with the FDA's proposed new regulatory framework for currently administered and newly developed LDTs would be untenable, given the time and cost of guiding even a single test through the FDA premarket approval process. Therefore, institutions will begin to budget for a certain number of LDTs and abandon others, to the detriment of patients. This cost would necessarily lead to institutional decisions that could limit patient access to innovative and targeted diagnostic tests.

CLIA Regulatory Framework for LDTs

The release of the FDA 2014 guidance prompted the discussion and development of several alternative proposals from stakeholder organizations and legislators. The goals of these efforts generally tried to ensure the validity and utility of LDTs without slowing innovation, creating an overly burdensome and expensive process, or jeopardizing patient care and advances in personalized medicine. These alternative proposals differ in whether the FDA or CMS should maintain primary responsibility for LDT oversight and also demonstrate different approaches to classifying tests based on risk. Those alternative frameworks that propose an expanded role for CMS note that LDTs, while currently not regulated by the FDA, are subject to some level of oversight through CLIA. More “CLIA-centric” proposals suggest that CMS’ role should be expanded by investing additional federal resources in CMS and modernizing CLIA to give greater oversight responsibility and enforcement authority over LDTs. Others suggested a blended approach, where certain tests, such as those deemed very high risk or containing proprietary information are automatically or voluntarily submitted to the FDA for approval, while the vast majority of LDTs would either be regulated through an expanded CLIA framework or not subject to additional regulation. While a theoretical alternative to FDA regulation, both CMS and FDA have been clear¹ that neither agency would support this approach, making a workable solution less likely.

A Path Forward for LDT Regulation

The regulations of all LDTs at AMCs will not address what the FDA posits is a public health risk. Instead, the FDA’s overbroad proposed regulation of LDTs will threaten the care patients expect to receive from AMCs. We have suggested to the FDA a tiered enforcement strategy that recognizes the risk mitigation factors present in LDTs developed by ACLs. However, should policymakers and regulators move forward with any form of LDT regulation without providing an exemption for ACLs, such regulatory framework must lessen the burden on ACLs by altering several previous policy proposals in order to make these new regulations less likely to decrease the number of available tests for patient care, potentially negatively impacting patients’ health. The most onerous and resource-intensive aspects of the LDT regulation could be diminished without increased risk to patients or access to care by ensuring that any regulatory framework applicable to labs that are designated as “academic clinical laboratories:”

- Grandfather in existing tests that have been successfully used for the benefit of patients at AMCs and exclude them from further regulation.
- Exclude ACLs from any requirement to proactively list all tests that are to be grandfathered. Instead, such labs should be prepared to present evidence of use of the test prior to enactment should a question arise about whether a test was properly included in this exemption.

¹ https://www.fda.gov/medical-devices/medical-devices-news-and-events/fda-and-cms-americans-deserve-accurate-and-reliable-diagnostic-tests-wherever-they-are-made?utm_medium=email&utm_source=govdelivery

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- Have every test developed by an ACL be designated as low-risk and not subject to the additional requirements for high-risk tests. This would acknowledge the risk-mitigating factors that arise from additional oversight, expertise, and integration into clinical care that ACLs demonstrate, aspects that are wholly different from commercial or reference labs.
- When a test is grandfathered, exempt from premarket review through a technology certification, or approved through premarket review, if that test is developed and administered by an ACL, any changes to the type of specimen used for the test would not be considered a modification that would cause it to be treated as a new test.

Conclusion

The AAMC appreciates your interest in examining the competing regulatory frameworks for the regulation of LDTs, alternative approaches to diagnostic test regulation at AMCs, and the impact on patient access to care and medical innovation. We look forward to continuing to work with you and other policymakers to ensure diagnostic tests are safe and readily available for patient care. If you have any further questions, please contact my colleague Len Marquez, Senior Director of Government Relations and Legislative Advocacy (lmarquez@aamc.org) or me.

Sincerely,



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